UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,877	08/02/2001	Jerry Y. Jonn	CMC 5024 USCIP1	4857

27777 7590 09/08/2009

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
CHOI, FRANK I	
ART UNIT	**PAPER NUMBER**
1616	

MAIL DATE	DELIVERY MODE
09/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/919,877	JONN ET AL.	
	Examiner	Art Unit	
	FRANK I. CHOI	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2006*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *74-93 and 95-102* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *74-93, 95-102* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

In view of the Supplemental Appeal Brief filed on 6/22/2009, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

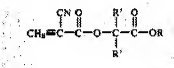
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 74-93, 95-102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark et al. (US Pat. 5,981,621) in view of Kronenthal et al. (US Pat. 3,995,641), Hammerslag

(US Pat. 6,386,203), EP 0 965 623, Leung (US Pat. 5,928,611) and Hawkins et al. (US Pat. 3,591,676).

Clark et al. teach a composition comprising at least two different monomers which form a medically acceptable polymer, at least one plasticizer and a mixture of anionic and radical stabilizers, such as, sulfur dioxide, hydroquinone, p-methoxyphenol and butylated hydroxyanisole (Column 2, lines 63-68, Columns 3-6, Claims 1, 7). It is taught that in applying the composition a polymerization initiator, such as benzalkonium chloride or tetrabutylammonium bromide, is used and may be readily selected by one of ordinary skill in the art without undue experimentation (Column 11, lines 18-68). Examples of suitable monomers include 2-octyl cyanocrylate, 2-isopropoxyethyl cyanoacrylate and alpha-cyanoacrylates disclosed in US Pat. 3,995,641 to Kronenthal et al. (Column 4, lines 7-68, Column 5, lines 1-65). It is disclosed that when using a strong acid as an acid stabilizer that a concentration range of 20-80 ppm can be used and that the maximum amount of sulfur dioxide should be 50 ppm, preferably less then 30 ppm (Column 6, lines 45-48, Column 7, lines 12-16).

Kronenthal et al. teaches carbalkoxyalkyl 2- cyanoacrylates which are readily assimilated by tissues and exhibit a relatively low degree of inflammatory tissue response (column 1, lines 60-68, Column 2, lines 1-11). It is disclosed that carbalkoxyalkyl 2-cyanoacrylates (0%, 25%, 17%, 26% polymer remaining after 16 weeks) biodegraded at a faster rate than isobutyl 2-cyanoacrylate (82% remaining after 16 weeks) (Column 13, lines 1-30). It is disclosed that the carbalkoxyalkyl 2-cyanoacrylates have the following formula (Column 2, lines 18-45):



wherein R is an organic radical and each R′ is individually hydrogen or methyl.

Organic radical R is not critical to the instant invention and may be any hydrocarbon radical, substituted or unsubstituted, which is convenient to the preparation and use of the carbalkoxyalkyl 2-cyanoacrylate adhesives of the instant invention. Radical R may be straight chain, branched or cyclic, saturated, unsaturated or aromatic.

Typical examples of such organic radicals include C_{1-8} alkyl radicals, C_{2-8} alkenyl radicals, C_{2-8} alkynyl radicals, C_{3-12} cycloaliphatic radicals, aryl radicals such as phenyl and substituted phenyl and aralkyl radicals such as benzyl, methylbenzyl and phenylethyl. Also included are substituted hydrocarbon radicals, particularly halo-, e.g., chloro-, fluoro- and bromo-substituted hydrocarbons, and oxy-, e.g., alkoxy substituted hydrocarbons. Preferred R radicals are alkyl, alkenyl and alkynyl radicals having from 1 to about 8 carbon atoms, and halo substituted derivatives thereof. Particularly preferred are alkyl radicals of 4 to 6 carbon atoms.

Hammerslag teaches that polymerizable cyanoacrylates can be co-polymerized with other compounds that alter elasticity, modify viscosity and aid in biodegradation (Column 5, lines 21-33). It is taught that suitable cyanoacrylates can be chosen from methyl, ethyl, butyl, methoxypropyl, alkoxyalkyl, and carbalkoxyalkyl depending on acceptable toxicity and other properties for a given application (Column 5, lines 54-67). It is taught that there is a wide variation in the rates of biodegradation of cyanocrylates but generally polymers of cyanoacrylates which have substituents that are small and/or contain one or more oxygen-containing functional groups appear to have increased biodegradability rates whereas cyanoacrylates having long chain alkyl groups lacking in oxygen-containing functional groups as substituents tend to form polymers which biodegrade more slowly (Column 6, lines 33-45). It is

taught that one or ordinary skill in the art would be able to by routine experimentation choose a cyanoacrylate with suitable biodegradation characteristics (Column 6, lines 49-56).

EP 0 965 623 teaches the combination of sulfuric acid and sulfur dioxide with free radical stabilizers for use in cyanoacrylate compositions to stabilize and enhance the shelf-life of said composition (Pg.4, lines 5-35, Pg. 5, lines 33-51). It is taught that suitable cyanoacrylates include 2-octyl cyanocrylate, 2-isopropoxyethyl cyanoacrylate and alpha-cyanoacrylates disclosed in US Pat. 3,995,641 to Kronenthal et al. (Pg. 9, Pg. 10, lines 1-28). It is disclosed that suitable radical stabilizing agents include hydroquinone, p-methoxy phenol and butylate hydroxyl anisole (BHA) and that the amount BHA can range from about 1,000-5,000 ppm (Paragraph 0081). An embodiment is disclosed containing between 20 and 40 ppm sulfur dioxide, 1500 ppm hydroxyquinoline, 145 ppm paramethoxyphenol and 1500 ppm acetic acid (Paragraph 0103).

Leung discloses a polymerizable material that can include one or more materials in mixture and that the material may be composed of monomers, including alpha-cyanoacrylate monomers, including 2-octyl alpha cyanoacrylate and the carbalkkoxy alkyl alpha-cyanoacrylate of US Pat. No. 3,995,641 to Kronenthal et al. (Column 4, lines 11-68, Column 6, Column 6, lines 1-49). It is disclosed that polymerization inihibitors can be present in an amount of 0 to 50, preferably 0.001 to 25 and more preferably 0.002 to 10 percent by weight (Column 7, lines 13-27). It is disclosed that polymerization initiators may be readily selected by one of ordinary skill in the art without undue experimentation and that suitable initiators include, cationic surfactants, such as tetrabutylammonium bromoide (Column 9, lines 42-48). An example is disclosed where the setting time of each of 2-octyl cyanoacrylate and 2-isopropoxyethyl cyanoacrylate was

reduced from greater than 240 seconds to less than a minute by addition of a polymerization inhibitor (Column 12, lines 5-40). It is disclosed that efforts to increase tissue compatibility of alpha cyanoacrylates having included modifying the alkyl ester group of the cyanoacrylates, for example, by increasing the alkyl ester chain link, e.g. butyl 2-cyanoacrylates and octyl-2-cyanocrylates, which has increased biocompatibility but the higher analogs biodegrade at slower rates than the lower alkyl cyanoacrylates (Column 1, lines 43-49). It is disclosed that other examples of modified alpha-cyanoacrylates used in biomedical applications include carbalkoxyalkyl alpha cyanoacrylates, for example, US Pat. 3,995,641 to Kronenthal et al., and alkoxyalkyl 2-cyanoacrylates, for example, US Pat. 3,559,652 to Bannitt et al. (Column 1, lines 50-56). It is disclosed that other efforts have included mixing alpha-cyanoacrylates with higher esters of 2-cyanoacrylic acid, for example, US Pat. 3,591,676 to Hawkins (Column 1, lines 56-60).

Hawkins discloses methyl 2-cyanoacrylate is readily biodegradeable whereas other types of surgical adhesives are not as readily biodegradable (Column 2, lines 9-30). The testing of a 50/50 mixture and a 25/75 mixture of methyl 2-cyanocrylate and n-butyl 2-cyanoacrylate is disclosed in which the 25/75 mixture exhibited greater retention time than the 50/50 mixture due to the presence of the higher amount of n-butyl 2-cyanoacrylate (Column 3, lines 10-42). It is disclosed that the testing demonstrates that mixtures of monomers can be used successfully as surgical adhesives (Column 3, lines 42-43).

Clark et al. disclose a composition comprising at least two different monomers which form a medically acceptable polymer, at least one plasticizer, a mixture of anionic and radical stabilizers, such as sulfur dioxide, hydroquinone, p-methoxyphenol and butylated

hydroxyanisole, a polymerization initiator, such as benzalkonium chloride or tetrabutylammonium bromide. The difference between Clark et al. and the claimed invention is that the prior art does not expressly disclose a composition or film having a first monomer, which includes alkyl ester cyanocrylate, and a different second monomer where the absorption rate of the first monomer species is different from the absorption rate of the second monomer species. However, the prior art amply suggests the same as the prior art discloses the combination of different monomers in forming medical adhesives. Further, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to combine an alkyl ester cyanoacrylate with a different cyanoacrylate, such as an octyl 2-cyanoacrylate or alkylether cyanoacrylate, with the expectation that biodegradation of the composition could be adjusted readily by modifying the ratio of the monomers and the composition would have a low degree of inflammatory response. Further, one of ordinary skill in the art would have been motivated to combine sulfur dioxide and sulfuric acid with radical stabilizers such as hydroquinone, p-methoxyphenol and butylated hydroxyanisole with the expectation that the composition would be more stable. Finally, one of ordinary skill in the art would have been motivated to use benzalkonium chloride or a bromide salt thereof with the expectation that it would act as a polymerization initiator and reduce the time of polymerization to under three minutes.

Examiner has duly considered Applicant's arguments but deems them moot in light of the new grounds of rejection herein.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Claims 74-93. 95-102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark et al. (US Pat. 5,981,621) in view of Kronenthal et al. (US Pat. 3,995,641), Hammerslag (US Pat. 6,386,203), EP 0 965 623, Banitt et al. (US Pat. 3,559,652), Collins et al., Leung (US Pat. 5,928,611) and Hawkins et al. (US Pat. 3,591,676).

Clark et al. (US Pat. 5,981,621), Kronenthal et al. (US Pat. 3,995,641), Hammerslag (US Pat. 6,386,203), EP 0 965 623, Leung (US Pat. 5,928,611) and Hawkins et al. (US Pat. 3,591,676).are cited for the same reasons as above and are incorporated herein to avoid repetition.

Banitt et al. teaches that alkoxyalkyl 2-cyanoacrylates are biodegradeable and have minimal toxicity (Column 1, lines 70-75, Column 2). It is disclosed that compared with alkyl 2-cyanoacrylates (1.2%, 9%), with the exception of methyl 2-cyanoacrylate (100% in 75 days), alkoxyalkyl 2-cyanocrylates (34% , 54.7%, 92.3%, 100% in 16 weeks) have a substantially higher rate of absorption by living tissue (Column 6, lines 45-75, Column 7, lines 1-10).

Collins et al. teach that the longer chained alkyl cyanoacrylates, such as octyl 2-cyanocrylate, are more effective tissue adhesives and hemostasis-inducing agents than the lower homologues because of their faster polymerization rate in blood, however, the higher homologues do not biodegrade as rapidly. (Pgs. 428, 429, 431). It is taught that the salutary combination of effectiveness in hemostasis inducing ability of the higher homologues and rapid

biodegradation of the methyl monomer would be highly desirable in a tissue adhesive (Pgs. 431, 432).

Clark et al. discloses a composition comprising at least two different monomers which form a medically acceptable polymer, at least one plasticizer, a mixture of anionic and radical stabilizers, such as sulfur dioxide, hydroquinone, p-methoxyphenol and butylated hydroxyanisole, a polymerization initiator, such as benzalkonium chloride or tetrabutylammonium bromide. The difference between Clark et al. and the claimed invention is that the prior art does not expressly disclose a composition or film having a first monomer, which includes alkyl ester cyanocrylate, and a alkyl alpha-cyanoacrylate second monomer where the absorption rate of the first monomer species is different from the absorption rate of the second monomer species. However, the prior art amply suggests the same as the prior art discloses the combination of different monomers in forming medical adhesives. Further, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to combine an alkyl ester cyanoacrylate with higher alkyl cyanoacrylate, such as octyl 2-cyanoacrylate, with the expectation that the composition would suitable for use as a tissue adhesive and hemostasis-inducing agent and with the expectation that the biodegradation rate could be adjusted readily by modifying the ratio of the monomers. Further, one of ordinary skill in the art would have been motivated to combine sulfur dioxide and sulfuric acid with radical stabilizers such as hydroquinone, p-methoxyphenol and butylated hydroxyanisole with the expectation that the composition would be more stable. Finally, one of ordinary skill in the art would have been motivated to use benzalkonium chloride or bromide salt thereof with the

expectation that it would act as a polymerization initiator and reduce the time of polymerization to under three minutes.

Examiner has duly considered Applicant's arguments but deems them moot in light of the new grounds of rejection.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Claims 74-93, 95-102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark et al. (US Pat. 5,981,621) in view of Berger et al. (US Pat. 5,998,472), Kronenthal et al. (US Pat. 3,995,641), Hammerslag (US Pat. 6,386,203), EP 0 965 623, Leung (US Pat. 5,928,611) and Hawkins et al. (US Pat. 3,591,676).

Berger et al discloses the mixture of reactive C1 to C8 cyanoacrylate ester monomer and a C10-C12 cyanoacrylate monomer to provide enhanced flexibility of the polymer film (Column 3, lines 1-54). It is disclosed that the term "C1 to C8 alkyl cyanoacrylate compositions" refers to polymerizable formulations comprising polymerizable cyanoacrylate ester monomers (Column 4, lines 60-68). It is disclosed that polymerizable cyanoacrylate ester monomers are known in the art and are described in US Pat. No. 3,995,641 to Kronenthal et al. (Column 1, lines 30, 31, Column 5, lines 31-44). It is disclosed that the cyanoacrylate composition can include an effective amount of a polymerization inhibitor, such as sulfur dioxide, glacial acetic acid, hydroquinone and hindered phenols (e.g., 4-methoxyphenol) and the like (Column 3, lines 63-68, Column 4, lines 1,2). It is disclosed that sulfur dioxide is preferably employed at from about 50 to 1000 ppm and that hydroquinone is preferably employed at about 50 to 250 ppm (Column 4,

lines 3-31, Column 6, lines 46-65). It is disclosed that mixtures of free radical polymerization inhibitors and acid polymerization inhibitors are often used (Column 6, lines 66, 67).

Kronenthal et al. (US Pat. 3,995,641), Hammerslag (US Pat. 6,386,203), Clark et al. (US Pat. 5,981,621), EP 0 965 623, Leung (US Pat. 5,928,611) and Hawkins et al. (US Pat. 3,591,676).are cited for the same reasons as above and are incorporated herein to avoid repetition.

Clark et al. discloses a composition comprising at least two different monomers which form a medically acceptable polymer, at least one plasticizer, a mixture of anionic and radical stabilizers, such as sulfur dioxide, hydroquinone, p-methoxyphenol and butylated hydroxyanisole, a polymerization initiator, such as benzalkonium chloride or tetrabutylammonium bromide. The difference between the prior art and the claimed invention is that the prior art does not expressly disclose combination of alkyl ester cyanocrylate and other alkyl alpha-cyanoacrylate monomer based on difference in biodegradation rate where the polymer has a different biodegradation rate than the monomers. However, the prior art amply suggests the same as the prior art discloses the combination of different monomers in forming medical adhesives. Further, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to combine an alkyl ester cyanoacrylate with a different cyanoacrylate, such as an C8-C12 alkyl cyanoacrylate, with the expectation that biodegradation of the composition could be adjusted readily by modifying the ratio of the monomers, that the composition would exhibit a low degree of inflammatory response and that the polymerized film would exhibit flexibility. Further, one of ordinary skill in the art would have been motivated to combine sulfur dioxide and sulfuric acid with radical stabilizers such as hydroquinone, p-

methoxyphenol and butylated hydroxyanisole with the expectation that the composition would be more stable. Finally, one of ordinary skill in the art would have been motivated to use benzalkonium chloride or bromide salt thereof with the expectation that it would act as a polymerization initiator and reduce the time of polymerization to under three minutes.

The Examiner has duly considered Applicant's arguments but deems them moot in light of the new grounds of rejection herein.

Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a compressed schedule and may be reached Monday, Tuesday, Wednesday and Thursday, 6:00 am – 4:30 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Johann R. Richter, can be reached at (571)272-0646. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frank Choi
Patent Examiner
Technology Center 1600
August 31, 2009

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617